Non-technical Abstract

A Phase I Study of Vaccination with Autologous, Lethally Irradiated Non-small Cell Lung Carcinoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor

No consistently effective therapy exists for metastatic non-small cell lung carcinoma (NSCLC). Recent studies have demonstrated that targets present on many NSCLC cells can elicit T cell and antibody responses in some patients. We have conducted extensive laboratory studies using a new strategy for augmenting anti-tumor immune responses to mouse tumors, including lung carcinoma. By inserting the immunostimulatory gene granulocyte-macrophage colony stimulating factor (GM-CSF) into mouse lung carcinoma tumor cells and injecting them under the skin, systemic anti-tumor immune responses have been induced, resulting in the eradication of implanted tumors at distant sites. Importantly, the tumor vaccine cells could be lethally irradiated after genetic engineering without compromising the efficacy of treatment. These effects have been observed in multiple murine tumors including melanoma, renal cell carcinoma, prostate carcinoma, colon carcinoma, bladder carcinoma, sarcoma, neuroblastoma, glioma, leukemia, and lymphoma.

Based on these studies, we have performed during the past two years a Phase I study in patients with metastatic melanoma of vaccination with lethally irradiated, autologous melanoma cell engineered by retroviral mediated gene transfer to secrete GM-CSF. This study has documented the consistent induction of potent anti-tumor immunity (associated with clinical benefit in a significant number of patients) without the development of significant toxicity. In the proposed study, we will attempt to extend these principles to NSCLC. Because of the complexity and length of producing vaccines with retroviral vectors, however, this study will examine the biologic activity of a greatly simplified method for vaccine preparation. In this trial, harvested tumor masses will be prepared to single cell suspension, infected overnight with an adenovirus expressing human GM-CSF, and then irradiated and frozen the following day.

The proposed study seeks to determine the safety and toxicity of administering this type of genetically engineered cancer vaccine. While the study is not intended to assess the efficacy of this treatment, it will provide important information that will be incorporated into future efficacy studies. Measurements will be made in this trial of any immunologic responses stimulated by the vaccine.